characteristics recited in previous claim 1, are administered to the patient.

Turning now the issues raised in the outstanding Official Action, previous claims 1 and 2 were rejected at item 2 thereof for indefiniteness, based on a perceived lack of clarity in the phrase "predetermined macrophages." The basis for that rejection is avoided in new claims 3-5, which do not use that term. Consequently, it is believed that the rejection of previous claims 1 and 2 for indefiniteness should not be repeated with respect to any of the new claims 3-5.

At item 3 of the Official Action, claim 1 was rejected as anticipated by CHOKRI et al. "Adoptive immunotherapy with bispecific antibodies: targeting through macrophages", Res. Immunol. 1992, 143, pp. 95-99. It is believed that none of new claims 3-5 is anticipated by CHOKRI et al. because that publication does not disclose or suggest macrophages having the characteristics claimed, much less the administration of such macrophages together with the claimed bispecific antibodies, in the context of a cancer treatment method.

In greater detail, CHOKRI concerns an anti-FcγRI/anti-RhD+ bispecific antibody and an anti FcγR1 bispecific antibody, and also a human adenocarcinoma antigen.

However, the macrophages of the earlier CHOKRI et al. article are not the same as, or obvious precursors of, the macrophages involved in the present method. In particular, the CHOKRI et al. macrophages do not have the characteristics

required by the new independent claim 3. The differences in properties of the macrophages are believed to arise from the different culturing conditions employed. For example, in the CHOKRI et al. article, the macrophages are cultured in a IMDM medium, whereas in the present specification the macrophages are cultured in the presence of GM-CSF and vitamin D_3.

Consequently, it is believed to be apparent that the CHOKRI et al. article cannot support a rejection of any of the new claims 3-5.

At items 4-6 of the Official Action, previous claims 1 and 2 were rejected as allegedly being anticipated by each of RING et al. 5,959,084; FANGER et al. 5,635,600; and Medarex, Inc. WO 91/058171. Those rejections are also respectfully traversed, at least to the extent they might be deemed to relate to any of the new claims 3-5.

RING concerns bispecific antibodies. One of them recognizes FcγRIII and the multi-drug resistance antigen, MDR (P-glycoprotein or gp 170). These bispecific antibodies are used to kill cancer cells.

FcγRIII is present on macrophages (column 2, line 62).

The cells used in this document are effective cytotoxic cells, for example leukocytes, NK cells or monocytes/macrophages, which have been isolated from blood (column 11, lines 34-55).

Activated macrophages are not cited, nor the preparation of effective cells. Actually, the cells are directly isolated from the blood and they are not differentiated *in vitro*.

Many cell types that are present in the cell preparation bind to the antibodies (column 21, lines 1-34).

In conclusion, the macrophages of this document do not have the same properties as the macrophages of the present invention.

FANGER concerns antibodies which bind to IgG receptors on mononuclear phagocytes without blocking the fixation of IgG to their receptor.

This document does not describe activated macrophages. Furthermore, the macrophages of the document are not characterized by their cytotoxicity.

The antibodies are used here to target effective cells, e.g., macrophages, for tumor target cells.

These antibodies can also be used to induce an ADCC (Antibody Dependent Cell-mediated Cytotoxicity)(column 3, line 15).

In conclusion, the macrophages of this document also do not have the same properties as the macrophages of the present invention.

WO 91/05871 concerns bispecific antibodies, which bind to the Fc receptor of effector cells (e.g., macrophages). (see abstract).

The target cells can be destroyed by ADCC (Antibody Dependent Cell-mediated Cytotoxicity) and fixation of the complement.

The preparation of the effector cells is described on page 11.

The macrophages described in this document are different from the macrophages of the present invention.

From the above discussion, therefore, it is believed to be apparent that none of the references applied at items 4-6 of the Official Action, against previous claims 1 and 2, can support a rejection of any of the new claims 3-5.

As regards support in the present specification for the new claims 4 and 5, this can be found, for example, at page 10, lines 6 and 7 of the specification.

In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with new claims 3-5. Allowance and passage to issue on that basis are accordingly respectfully requested.

Respectfully submitted,

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